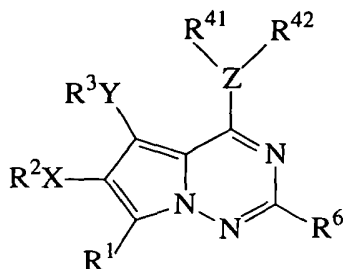


What is Claimed is:

1. A compound of formula (I):



(I)

5

or an enantiomer, diastereomer, or pharmaceutically acceptable salt, prodrug, or solvate thereof, wherein

- 10 Z is selected from O, S, N, OH, or Cl, with the provisos that when Z is O or S, R^{41} is absent and when Z is OH or Cl, both R^{41} and R^{42} are absent and when Z is N, then R^{41} is H;

X and Y are independently selected from O, OCO, S, SO, SO₂, CO, CO₂, NR¹⁰, NR¹¹CO, NR¹²CONR¹³, NR¹⁴CO₂, NR¹⁵SO₂, NR¹⁶SO₂NR¹⁷, SO₂NR¹⁸, CONR¹⁹, halogen, nitro, cyano, or X or Y are absent;

- 15 R¹ is hydrogen, CH₃, OH, OCH₃, SH, SCH₃, OCOR²¹, SOR²², SO₂R²³, SO₂NR²⁴R²⁵, CO₂R²⁶, CONR²⁷R²⁸, NH₂, NR²⁹SO₂NR³⁰R³¹, NR³²SO₂R³³, NR³⁴COR³⁵, NR³⁶CO₂R³⁷, NR³⁸CONR³⁹R⁴⁰, halogen, nitro, or cyano;

- 20 R² and R³ are independently hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heterocyclo, substituted heterocyclo, aralkyl, substituted aralkyl, heterocycloalkyl or substituted heterocycloalkyl, or when X is halo, nitro or cyano R² is absent or when Y is halo, nitro or cyano R³ is absent;

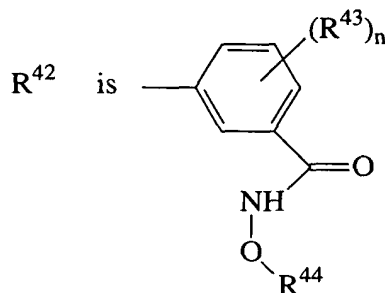
R⁶ is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, heterocyclo, substituted heterocyclo, NR⁷R⁸, OR⁹ or halogen;

- 25 R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸, R¹⁹, R²¹, R²⁴, R²⁵, R²⁶, R²⁷, R²⁸, R²⁹, R³⁰, R³¹, R³², R³⁴, R³⁵, R³⁶, R³⁸, R³⁹ and R⁴⁰ are independently selected

from the group consisting of hydrogen, alkyl, substituted alkyl, aryl,
substituted aryl, heterocyclo, or substituted heterocyclo;

R^{22} , R^{23} , R^{33} and R^{37} are independently selected from the group consisting of alkyl,
substituted alkyl, aryl, substituted aryl, heterocyclo, or substituted heterocyclo;

5 and



wherein

10 each R^{43} is independently selected from fluorine or methyl;

n is 0, 1 or 2; and

R^{44} is methyl, ethyl or cyclopropylmethyl;

with the further provisos that:

- 15 a. R^2 may not be hydrogen if X is SO , SO_2 , $NR^{13}CO_2$, or $NR^{14}SO_2$, and
b. R^3 may not be hydrogen if Y is SO , SO_2 , $NR^{13}CO_2$, or $NR^{14}SO_2$.

2. The compound of formula (I) according to Claim 1, selected from the
group consisting of:

20 5-(1-Methylethyl)pyrrolo[2,1-f][1,2,4]triazin-4(3H)-one-6-carboxylic acid
ethyl ester,

4-Chloro-[2,1-f][1,2,4]triazin-5-(1-Methylethyl)pyrrolo-6-carboxylic acid
ethyl ester,

4-Chloro-5-(1-methylethyl)-6-(5-methyl-2-oxazolyl)pyrrolo[2,1-
f][1,2,4]triazin,

25 4-[[3-[(Methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-
f][1,2,4]triazine-6-carboxylic acid ethyl ester,

- 4-[[2-Fluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazine-6-carboxylic acid ethyl ester,
- 4-[[2-Fluoro-5-[(methoxyamino)carbonyl]-4-methylphenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazine-6-carboxylic acid ethyl ester,
- 5 4-[[3-[(Methoxyamino)carbonyl]-4-methylphenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazine-6-carboxylic acid ethyl ester,
- 4-[[4-Fluoro-3-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazine-6-carboxylic acid ethyl ester,
- 10 4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazine-6-carboxylic acid ethyl ester,
- 4-[3-[(Methoxyamino)carbonyl]phenoxy]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazine-6-carboxylic acid, ethyl ester,
- 4-[2-Fluoro-3-[(methoxyamino)carbonyl]phenoxy]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazine-6-carboxylic acid, ethyl ester,
- 15 4-[[2-Fluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazine-6-carboxylic acid,
- N-Ethyl-4-[[2-fluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazine-6-carboxamide,
- N-[2-(Dimethylamino)ethyl]-4-[[2-fluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazine-6-carboxamide,
- 20 4-[[2-Fluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-N-(2-hydroxyethyl)-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazine-6-carboxamide,
- 4-[[3-[(Methoxyamino)carbonyl]-4-methylphenyl]amino]-N-methyl-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazine-6-carboxamide,
- 25 4-[[3-[(Methoxyamino)carbonyl]-4-methylphenyl]amino]-5-(1-methylethyl)-N-[2-(1-pyrrolidinyl)ethyl]pyrrolo[2,1-f][1,2,4]triazine-6-carboxamide,
- [4-[[3-[(Methoxyamino)carbonyl]-4-methylphenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid 2-(1-methyl-2-pyrrolidinyl)ethyl ester,
- 30 4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazine-6-carboxylic acid,

[4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid 3-(methylsulfonyl)propyl ester,

5 [4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid ethyl ester,

[4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid 3-(1-piperidinyl)propyl ester,

10 5-[[6-[5-(Difluoromethyl)-1,3,4-oxadiazol-2-yl]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-4-yl]amino]-2,4-difluoro-N-methoxybenzamide,

5-[[6-Ethoxy-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-4-yl]amino]-4-fluoro-N-methoxy-2-methylbenzamide,

5-[[6-Acetyl-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-4-yl]amino]-N-methoxy-2-methylbenzamide,

15 2,4-Difluoro-N-methoxy-5-[[5-(1-methylethyl)-6-(2-methyl-1H-1,2,4-triazol-3-yl)pyrrolo[2,1-f][1,2,4]triazin-4-yl]amino]benzamide,

2,4-Difluoro-N-methoxy-5-[[5-(1-methylethyl)-6-(1-methyl-1H-1,2,4-triazol-3-yl)pyrrolo[2,1-f][1,2,4]triazin-4-yl]amino]benzamide,

20 2,4-Difluoro-N-methoxy-5-[[5-(1-methylethyl)-6-[5-((methylsulfonyl)methyl]-1,3,4-oxadiazol-2-yl)pyrrolo[2,1-f][1,2,4]triazin-4-yl]amino]benzamide,

5-[[6-[5-[Difluoro(methylsulfonyl)methyl]-1,3,4-oxadiazol-2-yl]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-4-yl]amino]-2,4-difluoro-N-methoxybenzamide,

25 5-[[6-[5-(Dimethylamino)-1,3,4-oxadiazol-2-yl]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-4-yl]amino]-2,4-difluoro-N-methoxybenzamide,

[4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid 2-(1-methyl-1H-1,2,4-triazol-5-yl)ethyl ester,

30 [4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid, (1-methyl-4-piperidinyl)methyl,

[4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid, 3-(1H-1,2,3-triazol-1-yl)propyl ester,

5 [4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid, 2-(1H-1,2,3-triazol-1-yl)ethyl ester,

[4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid, 3-(6-methyl-2-pyridinyl)propyl ester

10 [4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid 2-(methylsulfonyl)ethyl ester,

[4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid (2-butyl-1H-imidazol-4-yl)methyl ester,

15

[4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid 2-(4-pyridinyl)ethyl ester,

[4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid 2-

20 (dimethoxyphosphinyl)ethyl ester,

[4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid (6-methyl-2-pyridinyl)methyl ester,

[4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid [(2S)-1-methyl-2-pyrrolidinyl]methyl ester,

25

[4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid (1-methyl-2-piperidinyl)methyl ester,

30 [4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid 1-methyl-4-piperidinyl ester,

- [4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid 4-pyridinylmethyl ester,
- [4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid 3-pyridinylmethyl ester,
- 5 [4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid 2-(2-pyridinyl)ethyl ester,
- [4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid 2-pyridinylmethyl ester,
- [4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid 2-(4-morpholinyl)ethyl ester,
- 10 [4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid 2-(1-methyl-2-pyrrolidnyl)ethyl ester,
- [4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid 2-(1-methyl-2-pyrrolidnyl)ethyl ester,
- 15 [4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid 1-methyl-3-pyrrolidnyl ester,
- [4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid 2-ethoxyethyl ester,
- 20 [4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid [5-[(dimethylamino)methyl]-2-furanyl]methyl ester,
- [4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid 2-(1-piperidinyl)ethyl ester,
- 25 [4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid 3-hydroxybutyl ester,
- 4-Fluoro-N-methoxy-3-[[5-(1-methylethyl)-6-(5-methyl-2-oxazolyl)pyrrolo[2,1-f][1,2,4]triazin-4-yl]amino]benzamide,
- 30 2,4-Difluoro-N-methoxy-5-[[5-(1-methylethyl)-6-(5-methyl-2-oxazolyl)pyrrolo[2,1-f][1,2,4]triazin-4-yl]amino]benzamide,

- 2-Fluoro-N-methoxy-5-[[5-(1-methylethyl)-6-(5-methyl-2-oxazolyl)pyrrolo[2,1-f][1,2,4]triazin-4-yl]amino]benzamide,
 N-Methoxy-2-methyl-5-[[5-(1-methylethyl)-6-(5-methyl-2-oxazolyl)pyrrolo[2,1-f][1,2,4]triazin-4-yl]amino]benzamide,
 5 4-Fluoro-N-methoxy-2-methyl-5-[[5-(1-methylethyl)-6-(5-methyl-2-oxazolyl)pyrrolo[2,1-f][1,2,4]triazin-4-yl]amino]benzamide,
 2-Chloro-N-methoxy-5-[[5-(1-methylethyl)-6-(5-methyl-2-oxazolyl)pyrrolo[2,1-f][1,2,4]triazin-4-yl]amino]benzamide,
 2,4-Difluoro-N-methoxy-5-[[5-(1-methylethyl)-6-(5-methyl-1,2,4-oxadiazol-
 10 3-yl)pyrrolo[2,1-f][1,2,4]triazin-4-yl]amino]benzamide,
 and pharmaceutically acceptable salts and prodrugs thereof.
3. A compound selected from the group consisting of
 [4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-
 15 methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid 3-(methylsulfonyl)propyl ester,
 [4-[[2,4-Difluoro-5-[(methoxyamino)carbonyl]phenyl]amino]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-6-yl]carbamic acid 3-(1-piperidiny)propyl ester,
 20 5-[[6-[5-(Difluoromethyl)-1,3,4-oxadiazol-2-yl]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-4-yl]amino]-2,4-difluoro-N-methoxybenzamide,
 2,4-Difluoro-N-methoxy-5-[[5-(1-methylethyl)-6-(2-methyl-1H-1,2,4-triazol-3-yl)pyrrolo[2,1-f][1,2,4]triazin-4-yl]amino]benzamide,
 2,4-Difluoro-N-methoxy-5-[[5-(1-methylethyl)-6-[5-
 25 [(methylsulfonyl)methyl]-1,3,4-oxadiazol-2-yl]pyrrolo[2,1-f][1,2,4]triazin-4-yl]amino]benzamide,
 5-[[6-[5-[Difluoro(methylsulfonyl)methyl]-1,3,4-oxadiazol-2-yl]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-4-yl]amino]-2,4-difluoro-N-methoxybenzamide,
 30 5-[[6-[5-(Dimethylamino)-1,3,4-oxadiazol-2-yl]-5-(1-methylethyl)pyrrolo[2,1-f][1,2,4]triazin-4-yl]amino]-2,4-difluoro-N-methoxybenzamide,

4-Fluoro-N-methoxy-3-[[5-(1-methylethyl)-6-(5-methyl-2-oxazolyl)pyrrolo[2,1-f][1,2,4]triazin-4-yl]amino]benzamide,

2,4-Difluoro-N-methoxy-5-[[5-(1-methylethyl)-6-(5-methyl-2-oxazolyl)pyrrolo[2,1-f][1,2,4]triazin-4-yl]amino]benzamide, and

5 2,4-Difluoro-N-methoxy-5-[[5-(1-methylethyl)-6-(5-methyl-1,2,4-oxadiazol-3-yl)pyrrolo[2,1-f][1,2,4]triazin-4-yl]amino]benzamide.

4. A pharmaceutical composition comprising at least one of the compounds of Claim 1 and a pharmaceutically acceptable carrier.

10

5. A pharmaceutical composition comprising at least one of the compounds of Claim 1 in combination with pharmaceutically acceptable carrier and an anti-cancer or cytotoxic agent.

15

6. The pharmaceutical composition as recited in Claim 5, wherein said anti-cancer or cytotoxic agent is selected from the group consisting of: linomide, inhibitors of integrin $\alpha v \beta 3$ function, angiostatin, razoxane, tamoxifen, toremifene, raloxifene, droloxifene, idoxifene, megestrol acetate, anastrozole, letrozole, borazole, exemestane, flutamide, nilutamide, bicalutamide, cyproterone acetate, gosereline acetate, leuprolide, finasteride, herceptin, metalloproteinase inhibitors, inhibitors of urokinase plasminogen activator receptor function, growth factor antibodies, growth factor receptor antibodies, bevacizumab, cetuximab, tyrosine kinase inhibitors, serine/threonine kinase inhibitors, methotrexate, 5-fluorouracil, purine, adenosine analogues, cytosine arabinoside, doxorubicin, daunomycin, epirubicin, idarubicin, 20 mitomycin-C, dactinomycin, mithramycin, cisplatin, carboplatin, nitrogen mustard, melphalan, chlorambucil, busulphan, cyclophosphamide, ifosfamide, nitrosoureas, thiotepa, vincristine, paclitaxel, docetaxel, epothilone analogs, discodermolide analogs, eleutherobin analogs, etoposide, teniposide, amsacrine, topotecan, irinotecan, 25 flavopyridols, proteasome inhibitors including bortezomib and biological response 30 modifiers.

7. A method for producing an antiangiogenic effect which comprises administering to a mammalian species in need thereof, an effective antiangiogenic producing amount of at least one of the compounds of Claim 1.

5 8. A method for producing a vascular permeability reducing effect which comprises administering to a mammalian species in need thereof an effective vascular permeability reducing amount of at least one of the compounds of Claim 1.

9. A method of inhibiting protein kinase activity of growth factor receptors
10 which comprises administering to a mammalian species in need thereof, an effective protein kinase inhibiting amount of at least one of the compounds of Claim 1.

10. A method of inhibiting tyrosine kinase activity of growth factor
receptors which comprises administering to a mammalian species in need thereof, an
15 effective tyrosine kinase inhibiting amount of at least one of the compounds of Claim 1.

11. A method for treating proliferative diseases, comprising administering to
a mammalian species in need thereof, a therapeutically effective amount of a
20 composition of Claim 4.

12. A method for treating cancer, comprising administering to a mammalian
species in need thereof, a therapeutically effective amount of a composition of Claim
4.

25 13. A method for treating inflammation, comprising administering to a
mammalian species in need thereof, a therapeutically effective amount of a
composition of Claim 4.

30 14. A method for treating autoimmune diseases, comprising administering to
a mammalian species in need thereof, a therapeutically effective amount of a
composition of Claim 4.

15. A method for treating proliferative diseases, comprising administering to mammalian species in need thereof, a therapeutically effective amount of a composition of Claim 5.

5

16. A method for treating cancer, comprising administering to a mammalian species in need thereof, a therapeutically effective amount of a composition of Claim 5.

10

17. A method for treating inflammation, comprising administering to a mammalian species in need thereof, a therapeutically effective amount of a composition of Claim 5.

15

18. A method for treating autoimmune diseases, comprising administering to a mammalian species in need thereof, a therapeutically effective amount of a composition of Claim 5.

20

19. A method for treating diseases associated with signal transduction pathways operating through growth factor receptors, which comprises administering to a mammalian species in need thereof a therapeutically effective amount of at least one of the compounds of Claim 1.

25

20. A compound selected from
3-Amino-4-fluoro-*N*-methoxybenzamide,
5-amino-2-methyl-4-fluoro-*N*-methoxybenzamide,
5-amino-2-methyl-*N*-methoxycarboxamide, or
5-amino-2,4-difluoro-*N*-methoxybenzamide.